UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/597,517	06/20/2000	Thangavel Kuberasampath	CIBT-P07-503	5819

28120 7590 07/30/2002

ROPES & GRAY
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER
KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/30/2002 15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/597,517	KUBERASAMPATH ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,23 and 49-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,23 and 49-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Applications, Amendments, And/Or Claims

The amendment filed 06 June 2002 (Paper No. 13) has been entered in full. Claims 1, 2, 4-22 and 24-48 are canceled. Claims 3, 23, and 49-70 are under examination.

The formal drawings submitted with the response (Paper No. 13, 06 June 2002) are accepted.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

35 U.S.C. § 112, First Paragraph

Claims 3, 23 and 49-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pp. 2-3 of the previous Office Action (Paper No. 10, 28 January 2002).

Claims 3, 23 and 49-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pp. 3-4 of the previous Office Action (Paper No. 10, 28 January 2002).

Applicant's arguments (pp. 7-11, Paper No. 13, 06 June 2002) have been fully considered but are not found to be persuasive for the following reasons.

Applicant refers to several specific places in the specification (pp. 39, 54 and 57) that provides written description and enablement of the agents recited in the claims. Applicant also refers to Example 15 as providing written description and enablement of an assay that can be used to screen for the agents recited in the claims. This has been fully considered but is not found to be persuasive. The claims refer to a class of compounds ("agents") which stimulate *in vivo* a therapeutically effective concentration of an endogenous morphogen. This class is not structurally limited to any specific type of compound, and thus reads on proteins, agonistic antibodies, large organic molecules, small organic compounds, inorganic molecules, mimetics, minerals, vitamins, etc. The specification only refers to the class of "agents" as a whole, and then briefly mentions that a morphogen can be capable of stimulating endogenous morphogen production. In terms of written description, a single type of protein (morphogen) is not representative of the class of "agents" recited in the claims. Furthermore, the assay for identifying agents provided by Example 15 is limited to an assay for identifying agents that increase morphogen production by a ell in culture. The cultured cells are not accepted model systems for the diseases recited in the claims, nor are the morphogen levels produced by the cells tested for "therapeutically effective concentrations" as required by the claims. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The agent itself is

required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Applicant also argues that the specification need not teach what is well known in the art. Applicant refers to Laufer et al. (1994), Wall and Hogan (1994) and Roberts et al. (1995) as demonstrating that one skilled in the art was aware of factors which induce TGFβ expression *in vivo*. Specifically, Laufer et al. is provided as evidence that sonic hedgehog (a protein) induces expression of endogenous BMP-2 (a morphogen). This evidence has been fully considered but is not found to be persuasive. Laufer et al. discloses that sonic hedgehog induces BMP-2 expression in developing limb buds in a positive feedback loop. However, this developmental study has no bearing on the instant claims, which require administration of an agent that induces endogenous morphogen production to therapeutically effective levels in a diseased patient. There is no indication, for example, that sonic hedgehog has any effect on BMP-2 production in adult tissues, in diseased cells, or that the BMP-2 production would be effective to alleviate any of the symptoms of the diseased patient. Furthermore, Laufer et al. was published in 1994. The instant application claims priority to March of 1991. Therefore, what was disclosed in Laufer et al. was not well known in the art at the time of the invention, and applicant cannot rely on Laufer et al. as supporting enablement of the claimed invention.

Applicant refers to Roberts et al. (1994) as demonstrating a similar relationship between hedgehog protein and BMP expression in the gut after infection. This has been fully considered but is not found to be persuasive. Again, the instant application

claims priority to March of 1991. Therefore, what was disclosed in Roberts et al. in 1994 was not well known in the art at the time of the invention, and applicant cannot rely on Roberts et al. as supporting enablement of the claimed invention. Furthermore, Roberts et al. is not focused on hedgehog induction of BMP expression in response to infection. Roberts et al. discloses a developmental study of chick hindgut formation. The "infection" referred to in Roberts et al. is not a pathological infection, but rather an infection with a retroviral vector engineered to express a full-length cDNA of chicken sonic. The Roberts et al. infection was a retroviral misexpression study and had nothing whatsoever to do with pathological infection as recited in the claims (see Roberts et al. p. 3165, second paragraph of left hand column, and Figure 2B). Roberts et al. never disclose administration of a hedgehog protein to induce therapeutically effective amounts of a morphogen in a diseased patient, as required by the claims. The developmental studies of Laufer et al. and Roberts et al. would not be accepted by the skilled artisan as predictive of a therapy method.

Applicant refers to Wall and Hogan (1994), a review article, as evidence that factors which regulate TGFβ were well known in the art. This is not found to be persuasive, because Wall and Hogan are limited to a review on developmental studies, which are not predictive of therapy methods as argued above. Also, what was disclosed in Wall and Hogan in 1994 was not well known in the art at the time of the invention (1991), and applicant cannot rely on Wall and Hogan as supporting enablement of the claimed invention.

Applicant argues that the claims are not directed to the agents themselves, but rather to methods of using agents which induce morphogen expression. This has been fully considered but is not found to be persuasive. In order to practice the claimed invention, the skilled artisan would have to have knowledge of compounds that meet the limitations of the agents recited in the claims. This is in contrast to methods of identifying or screening for such agents. For such methods, the skilled artisan need only have knowledge of how to measure morphogen production and access to a library of potential agents. However, reach-through claims to the agents or the methods of administering the agents are not enabled, nor provided with adequate written description, in the instant application as originally filed.

New Rejections

Claims 50-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new mater rejection.

The newly submitted claims are directed to methods of treating specific diseases or conditions comprising administering an agent that stimulates *in vivo* a therapeutically effective concentration of a morphogen. The specification as originally filed provides written description of some of these specific conditions, such as psoriasis, but does not appear to address others (e.g., asthma, glomerular nephritis, etc.). Furthermore,

whereas the specification does discuss treatment of some of theses specific diseases or conditions by administration of a morphogen *per se*, it does not appear to provide written description of treatment of the specific conditions by administration of an agent that stimulates *in vivo* a therapeutically effective concentration of a morphogen. Applicant is required to either indicate where such is described in the specification as originally filed (precisely, with page and line indications) or cancel the claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Mon.-Thurs. and alternate Fri., 6:30-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ECK
July 29, 2002

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER